

of said extracted RNA comprises a tumor-derived or tumor-specific RNA species that is epidermal growth factor RNA, epidermal growth factor receptor (erb-B-1) RNA, her-2/neu RNA, c-myc RNA, heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof;

b) amplifying or signal amplifying said fraction of the extracted RNA or corresponding cDNA prepared therefrom, wherein amplification is performed [in] either [a] qualitatively or quantitatively [fashion] using primers or probes specific for the tumor-derived or tumor-associated RNA or cDNA corresponding thereto to produce an amplified product; and

c) detecting the amplified product produced from the RNA or cDNA.

2. (Amended) A method for detecting extracellular tumor-derived or tumor-associated RNA in a non-cellular fraction of a bodily fluid from a human or animal, wherein the tumor-derived or tumor-associated RNA is epidermal growth factor RNA, epidermal growth factor receptor (erb-B-1) RNA, her-2/neu RNA, c-myc RNA, heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof, the method comprising the steps of:

a) extracting mammalian total RNA from a non-cellular fraction of a bodily fluid, wherein a fraction of said extracted RNA comprises an extracellular tumor-derived or tumor-specific RNA species that is epidermal growth factor RNA, epidermal growth factor receptor (erb-B-1) RNA, her-2/neu RNA, c-myc RNA, heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof;

b) amplifying or signal amplifying said fraction of the extracted RNA or cDNA corresponding thereto, wherein amplification is performed [in] either [a] qualitatively or quantitatively [fashion] using primers or probes specific for the tumor-derived or tumor-associated RNA or cDNA corresponding thereto to produce an amplified product; and

c) detecting the amplified product produced from the RNA or cDNA corresponding thereto.

8. (Amended) The method of claim 2, wherein the RNA in step (a) is extracted from a non-cellular fraction of a bodily fluid using an RNA extraction method that is a gelatin extraction method; silica, glass bead, or diatom extraction method; guanidine-thiocyanate-phenol solution extraction method; guanidinium thiocyanate acid-based extraction method; phenol-chloroform-based extraction method; or involves centrifugation through a cesium chloride or similar gradient.

9. (Amended) The method for screening an animal or human for malignancy or premalignancy associated with epidermal growth factor RNA, epidermal growth factor receptor (erb-B-1) RNA, her-2/neu RNA, c-myc RNA, or heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof, the method comprising the steps of performing the method of claim 1 qualitatively or quantitatively, and detecting a product produced by said RNA in the plasma or serum of said animal or human, wherein detection of said RNA indicates that malignant or premalignant cells are present in the body of said animal or human.

10. (Amended) The method for screening an animal or human for malignancy or premalignancy associated with epidermal growth factor RNA, epidermal growth factor receptor (erb-B-1) RNA, her-2/neu RNA, c-myc RNA, or heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof, the method comprising the steps of performing the method of claim 2 qualitatively or quantitatively, and detecting a product produced by said RNA in the plasma or serum of said animal or human, wherein detection of said RNA indicates that malignant or premalignant cells are present in the body of said animal or human.

21. (Amended) A method for monitoring an animal or human for a malignant or premalignant disease, wherein the malignant or premalignant disease is associated with a tumor-derived or tumor-associated RNA that is epidermal growth factor RNA, epidermal growth factor receptor (erb-B-1) RNA, her-2/neu RNA, c-myc RNA, or

heterogeneous nuclear ribonucleoprotein A2/B1 RNA, or any combination thereof, the method comprising the step of:

[1) detecting RNA associated with the malignant or premalignant disease qualitatively or quantitatively, wherein the RNA is epidermal growth factor RNA, epidermal growth factor receptor (erb-B-1) RNA, her-2/neu RNA, c-myc RNA, or heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof, according to a method comprising the steps of:]

- a) extracting mammalian total RNA from plasma or serum, wherein a fraction of said extracted RNA comprises epidermal growth factor RNA, epidermal growth factor receptor (erb-B-1) RNA, her-2/neu RNA, c-myc RNA, heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof;
- b) amplifying or signal amplifying said fraction of the extracted RNA or corresponding cDNA, wherein amplification is performed qualitatively or quantitatively using primers or probes specific for the tumor-derived or tumor-associated RNA or cDNA corresponding thereto, to produce an amplified product; and
- c) detecting the amplified product produced from RNA or cDNA corresponding thereto.

36. (Amended) A method for selecting an animal or human with cancer for a cancer-directed therapy, the method comprising the steps of:

- a) extracting mammalian total RNA from plasma or serum of the animal or human, wherein a fraction of said extracted RNA comprises a tumor-derived or tumor-specific RNA that is epidermal growth factor RNA, epidermal growth factor receptor (erb-B-1) RNA, her-2/neu RNA, c-myc RNA, or heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof;
- b) amplifying or signal amplifying said fraction of the extracted RNA or cDNA corresponding thereto, wherein amplification is performed qualitatively or quantitatively using primers or probes specific for the tumor-derived or tumor-associated RNA or cDNA corresponding thereto to produce an amplified product; and

c) detecting the amplified product produced from said RNA or cDNA, whereby detection thereof selects the human with cancer for a cancer directed therapy.

37. (Amended) A method according to claim 1, further comprising the step of performing a diagnostic test for diagnosing cancer or premalignancy when epidermal growth factor RNA, epidermal growth factor receptor (erb-B-1) RNA, her-2/neu RNA, c-myc RNA, heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof is detected in plasma or serum of an animal or human.

40. (Amended) A method for monitoring response to an anticancer therapy, comprising the step of performing the method of claim 1 on blood plasma or serum from an animal or human with cancer to whom anticancer therapy is administered, and wherein response to the anticancer therapy is accomplished by qualitative or quantitative detection of epidermal growth factor RNA, epidermal growth factor receptor (erb-B-1) RNA, her-2/neu RNA, c-myc RNA, heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof.

41. (Amended) A method for monitoring response to an anticancer therapy, comprising the step of performing the method of claim 1 on blood plasma or serum from an animal or human with cancer to whom anticancer therapy is administered, and wherein response to the anticancer therapy is accomplished by qualitative or quantitative detection of epidermal growth factor RNA, epidermal growth factor receptor (erb-B-1) RNA, her-2/neu RNA, c-myc RNA, heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof.

51. (Amended) A diagnostic kit comprising primers specific for amplifying heterogeneous nuclear ribonucleoprotein A2/B1 RNA or cDNA prepared therefrom and reagents for extracting total RNA from an acellular fraction of a bodily fluid according to the method of claim 2.

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1. (Amended) A method for detecting tumor-derived or tumor-associated RNA in the plasma or serum fraction of blood from a human or animal, wherein the tumor-derived or tumor-associated RNA is epidermal growth factor RNA, epidermal growth factor receptor (erb-B-1) RNA, her-2/neu RNA, c-myc RNA, heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof, the method comprising the steps of:

a) extracting mammalian total RNA from plasma or serum, wherein a fraction of said extracted RNA comprises a tumor-derived or tumor-specific RNA species that is epidermal growth factor RNA, epidermal growth factor receptor (erb-B-1) RNA, her-2/neu RNA, c-myc RNA, heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof;

b) amplifying or signal amplifying said fraction of the extracted RNA or corresponding cDNA prepared therefrom, wherein amplification is performed either qualitatively or quantitatively using primers or probes specific for the tumor-derived or tumor-associated RNA or cDNA corresponding thereto to produce an amplified product; and

c) detecting the amplified product produced from the RNA or cDNA.

2. (Amended) A method for detecting extracellular tumor-derived or tumor-associated RNA in a non-cellular fraction of a bodily fluid from a human or animal, wherein the tumor-derived or tumor-associated RNA is epidermal growth factor RNA, epidermal growth factor receptor (erb-B-1) RNA, her-2/neu RNA, c-myc RNA, heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof, the method comprising the steps of:

a) extracting mammalian total RNA from a non-cellular fraction of a bodily fluid, wherein a fraction of said extracted RNA comprises an extracellular tumor-derived or tumor-specific RNA species that is epidermal growth factor RNA, epidermal growth

factor receptor (erb-B-1) RNA, her-2/neu RNA, c-myc RNA, heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof;

b) amplifying or signal amplifying said fraction of the extracted RNA or cDNA corresponding thereto, wherein amplification is performed either qualitatively or quantitatively using primers or probes specific for the tumor-derived or tumor-associated RNA or cDNA corresponding thereto to produce an amplified product; and

c) detecting the amplified product produced from the RNA or cDNA corresponding thereto.

8. (Amended) The method of claim 2, wherein the RNA in step (a) is extracted from a non-cellular fraction of a bodily fluid using an RNA extraction method that is a gelatin extraction method; silica, glass bead, or diatom extraction method; guanidine-thiocyanate-phenol solution extraction method; guanidinium thiocyanate acid-based extraction method; phenol-chloroform-based extraction method; or involves centrifugation through a cesium chloride or similar gradient.

9. (Amended) The method for screening an animal or human for malignancy or premalignancy associated with epidermal growth factor RNA, epidermal growth factor receptor (erb-B-1) RNA, her-2/neu RNA, c-myc RNA, or heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof, the method comprising the steps of performing the method of claim 1 qualitatively or quantitatively, and detecting a product produced by said RNA in the plasma or serum of said animal or human, wherein detection of said RNA indicates that malignant or premalignant cells are present in the body of said animal or human.

10. (Amended) The method for screening an animal or human for malignancy or premalignancy associated with epidermal growth factor RNA, epidermal growth factor receptor (erb-B-1) RNA, her-2/neu RNA, c-myc RNA, or heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof, the method comprising the

steps of performing the method of claim 2 qualitatively or quantitatively, and detecting a product produced by said RNA in the plasma or serum of said animal or human, wherein detection of said RNA indicates that malignant or premalignant cells are present in the body of said animal or human.

21. (Amended) A method for monitoring an animal or human for a malignant or premalignant disease, wherein the malignant or premalignant disease is associated with a tumor-derived or tumor-associated RNA that is epidermal growth factor RNA, epidermal growth factor receptor (erb-B-1) RNA, her-2/neu RNA, c-myc RNA, or heterogeneous nuclear ribonucleoprotein A2/B1 RNA, or any combination thereof, the method comprising the step of:

- a) extracting mammalian total RNA from plasma or serum, wherein a fraction of said extracted RNA comprises epidermal growth factor RNA, epidermal growth factor receptor (erb-B-1) RNA, her-2/neu RNA, c-myc RNA, heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof;
- b) amplifying or signal amplifying said fraction of the extracted RNA or corresponding cDNA, wherein amplification is performed qualitatively or quantitatively using primers or probes specific for the tumor-derived or tumor-associated RNA or cDNA corresponding thereto, to produce an amplified product; and
- c) detecting the amplified product produced from RNA or cDNA corresponding thereto.

35 36. (Amended) A method for selecting an animal or human with cancer for a cancer-directed therapy, the method comprising the steps of:

- a) extracting mammalian total RNA from plasma or serum of the animal or human, wherein a fraction of said extracted RNA comprises a tumor-derived or tumor-specific RNA that is epidermal growth factor RNA, epidermal growth factor receptor (erb-B-1) RNA, her-2/neu RNA, c-myc RNA, or heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof;

b) amplifying or signal amplifying said fraction of the extracted RNA or cDNA corresponding thereto, wherein amplification is performed qualitatively or quantitatively using primers or probes specific for the tumor-derived or tumor-associated RNA or cDNA corresponding thereto to produce an amplified product; and

c) detecting the amplified product produced from said RNA or cDNA, whereby detection thereof selects the human with cancer for a cancer directed therapy.

~~36~~ 37. (Amended) A method according to claim 1, further comprising the step of performing a diagnostic test for diagnosing cancer or premalignancy when epidermal growth factor RNA, epidermal growth factor receptor (erb-B-1) RNA, her-2/neu RNA, c-myc RNA, heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof is detected in plasma or serum of an animal or human.

40. (Amended) A method for monitoring response to an anticancer therapy, comprising the step of performing the method of claim 1 on blood plasma or serum from an animal or human with cancer to whom anticancer therapy is administered, and wherein response to the anticancer therapy is accomplished by qualitative or quantitative detection of epidermal growth factor RNA, epidermal growth factor receptor (erb-B-1) RNA, her-2/neu RNA, c-myc RNA, heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof.

41. (Amended) A method for monitoring response to an anticancer therapy, comprising the step of performing the method of claim 1 on blood plasma or serum from an animal or human with cancer to whom anticancer therapy is administered, and wherein response to the anticancer therapy is accomplished by qualitative or quantitative detection of epidermal growth factor RNA, epidermal growth factor receptor (erb-B-1) RNA, her-2/neu RNA, c-myc RNA, heterogeneous nuclear ribonucleoprotein A2/B1 RNA or any combination thereof.

51. (Amended) A diagnostic kit comprising primers specific for amplifying heterogeneous nuclear ribonucleoprotein A2/B1 RNA or cDNA prepared therefrom and reagents for extracting total RNA from an acellular fraction of a bodily fluid according to the method of claim 2.

52. (Amended) A method for producing cDNA by reverse transcription of a fraction of extracellular mammalian total RNA extracted from plasma or serum, wherein the fraction comprises epidermal growth factor RNA, epidermal growth factor receptor (erb-B-1) RNA, her-2/neu RNA, c-myc RNA, heterogeneous nuclear ribonucleoprotein A2/B1 RNA, or any combination thereof, whereby cDNA corresponding to said RNA is produced.

53.(Amended) A method for producing cDNA by reverse transcription of a fraction of extracellular mammalian RNA extracted from an acellular fraction of a bodily fluid, wherein the fraction comprising epidermal growth factor RNA, epidermal growth factor receptor (erb-B-1) RNA, her-2/neu RNA, c-myc RNA, heterogeneous nuclear ribonucleoprotein A2/B1 RNA, or any combination thereof, whereby cDNA corresponding to said RNA is produced.